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Craniosynostosis, Microcephaly, Hydrancephaly, Humero-Radial Synostosis, and Thumb Aplasia: A New Syndrome?

Greg Samson and Jessica C. Gardner

Department of Neonatology, Mowbray Maternity Hospital, Mowbray (G.S.), and MRC Unit for Medical Genetics, Department of Human Genetics, University of Cape Town, Medical School, Observatory (J.G.), South Africa

We describe a growth-retarded newborn infant with craniosynostosis, microcephaly, hydrancephaly, oligodactyly, humero-radial synostosis, and normal chromosomes. The combination of anomalies has hitherto been unreported and we consider this to be a "new" syndrome. © 1996 Wiley-Liss, Inc.

KEY WORDS: craniosynostosis, microcephaly, hydrancephaly, humero-radial synostosis, thumb aplasia

CLINICAL REPORT

A male infant of South African Xhosa ancestry was born in 1994 by normal vertex delivery to a 22-year-old gravida 2, para 1 mother following an uneventful pregnancy. Both parents were healthy and nonconsanguineous. The family history was unremarkable and there was no history of exposure to teratogenic agents during pregnancy.

The birthweight of the infant was 1,420 g at an estimated gestational age of 34 weeks. Clinical manifestations (Figs. 1, 2) included microbrachycephaly with an occipitofrontal circumference of 22 cm (<3rd centile), sloping of the forehead, and ridging of all sutures with an impalpable anterior but large posterior fontanel. The eyes were prominent with small palpebral fissures. The ears were apparently low-set and posteriorly angulated. Microstomia was evident together with micrognathia and markedly restricted movement of the mandible.

Fixed flexion contractures were present at both elbow and knee joints and were particularly striking in the former (Fig. 3). The thumbs were absent and the fifth fingers were short with no flexion creases (Fig. 4). A single transverse palmar crease was present on each hand.

The feet were mildly abnormal with small halluces, sandal gaps, and shortness of the 4th and 5th digits, bilaterally.

A 2/6 pansystolic murmur which was loudest at the lower left sternal border was clinically evaluated as a ventricular septal defect. The abdomen was ostensibly normal.

Radiographs of the skull showed complete sutural stenosis and a large posterior fontanel (Fig. 5). Craniosynostosis was confirmed on computerized axial tomography (CT scan). In addition, a gross malformation of the brain was noted with hydrancephaly (Fig. 6) and

Fig. 1. Frontal view of the affected child showing small palpebral fissures, sloping forehead, abnormal ears, micrognathia, prominence of metopic suture.

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Address reprint requests to Dr. Greg Samson, Department of Neonatology, Mowbray Maternity Hospital, Mowbray 7705, Republic of South Africa.

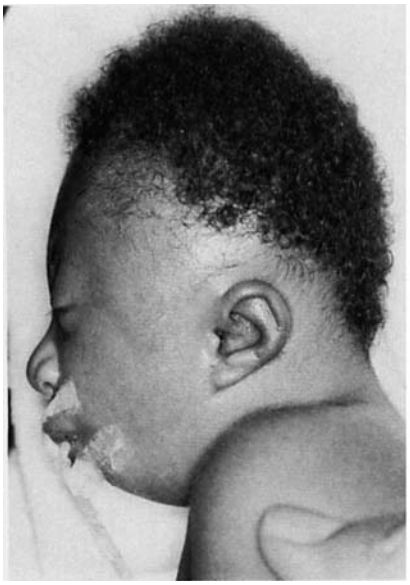

Fig. 2. Lateral view demonstrating microbrachycephaly, marked micrognathia, and small, simple ears.

Fig. 4. The right hand: absent thumb, single transverse palmar crease, and lack of flexion creases on the 5th finger.

poorly defined brain parenchyma at the base of the skull (Fig. 7). Radiographs of the upper limbs demonstrated the presence of bilateral humero-radial synostosis (Fig. 8) and absence of the middle phalanx in the fifth fingers. Despite the flexion contractures at the knees, there was no bony union between the femora and the tibiae. Chromosomes were apparently normal (46,XY).

The infant was hospitalized for 51 days, during which time he remained fully conscious and responsive to tactile and painful stimuli. He continued to thrive and was discharged from hospital, weighing 1,970 g. The infant subsequently died at home. Parental permission for autopsy was not granted.

DISCUSSION

The infant described in this report presented with a constellation of congenital anomalies that do not conform to those of any well established syndrome. The most notable clinical findings were craniosynostosis, microbrachycephaly, hydrancephaly, intrauterine growth retardation, absent thumbs, and radio-humeral synostosis. Several of the abnormalities including the arthrogryposis, the single palmar crease, micrognathia, and

Fig. 3. The affected infant: flexion contractures are present in the upper and lower limbs.

Fig. 5. Lateral skull radiograph showing complete craniosynostosis, absent anterior fontanel, and a large posterior fontanel.

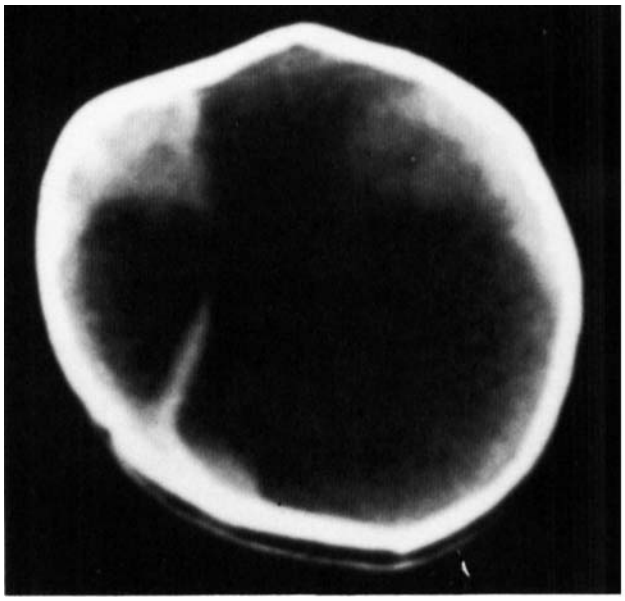

Fig. 6. Axial computerised tomogram of the brain showing the presence of hydrancephaly.

Fig. 8. Radiograph of the right arm depicting radio-humeral synostosis and absence of 1st ray.

the limitation in movement of the mandible may have been secondary to the severe CNS malformation.

The association of limb anomalies with craniosynostosis occurs as part of the clinical spectrum of a number of multiple malformation syndromes, including the Baller-Gerold [Dallapiccola et al., 1992], Roberts [Huson et al., 1990], Neu-Laxová [Seemanová and Rudolph, 1985], Herrmann [Herrmann et al., 1969], and Antley-Bixler syndromes [Gorlin et al., 1990], amongst others. However, the combination of craniofacial and skeletal anomalies in the South African infant were sufficiently distinct as to exclude these entities from the diagnosis.

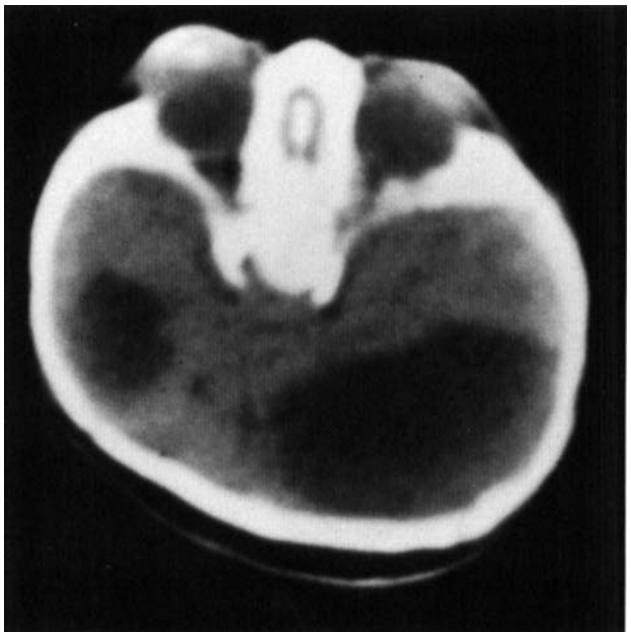

Fig. 7. Axial computerised tomogram of the head showing malformation of the brain with poorly defined parenchyma at the base of the skull.

Three private syndromes which featured prominently in our initial differential diagnosis of the unusual findings in our patient were those described by Ives and Houston [1980], Newbury-Ecob et al. [1993], and Imaizumi and Kuroki [1991]. The clinical manifestations in these syndromes are shown together with those of the South African infant in Table I.

The Ives-Houston syndrome, a lethal autosomal recessive disorder, is characterized by intrauterine growth retardation, marked microcephaly, craniosynostosis, severe limb malformations, fused elbows, and oligodactyly. The limb abnormalities presents with markedly short forearms, often with only a single bone present, and digits which were hypoplastic and grossly abnormal. Autopsies on these infants showed a small brain with primary sulci and gyri only, and absence of the corpus callosum in some cases. The intracranial findings in the South African boy differed in that he had marked hydrancephaly with gross malformation of the brain noted on CT scan. The precise nature of the abnormality could not be fully elucidated without the benefit of an autopsy. The differences in skeletal and intracranial findings were sufficient to suggest that the diagnosis of the Ives-Houston syndrome was unlikely in our patient.

Newbury-Ecob et al. [1993] described a male fetus with multiple congenital anomalies, including synostosis of the lambdoid sutures and many facial changes in common with our patient. Both affected individuals had hypertelorism, short palpebral fissures, prominent orbits, and micrognathia.

TABLE I. Comparison of Manifestations in the Southern African Infant and the Syndromes Documented by Ives and Houston [1980], Newbury-Ecob et al. [1993], and Imaizumi and Kuroki [1991]

	Present case	Ives-Houston syndrome [1980]	Newbury-Ecob et al. [1993]	Imaizumi and Kuroki [1991]
Intrauterine growth retardation	+	+	+	+
Craniosynostosis	+	+	+	−
Humero-radial synostosis	+	+	−	−
Thumb aplasia/abnormal fingers	+	+	+	+
Cerebral malformation	+	+	−	−
Malformed ears	+	−	+	+
Prominent eyes	+	−	+	+
Micrognathia	+	+	+	+
Microstomia	+	+	−	−
Arthrogryposis	+	−	−	−

The limb anomalies differed in that the Newbury-Ecob fetus had bilateral radius aplasia with small proximally placed thumbs, whereas the South African boy had absent thumbs and radiohumeral synostosis. Features which the Newbury-Ecob patient had and our infant lacked were talipes equino-varus, an anteriorly placed anus, and underdeveloped scrotum.

Newbury-Ecob et al. [1993] compared their findings with those of Imaizumi and Kuroki [1991], who described a Japanese boy with radial ray defects, dwarfism, a triangular face, and telecanthus. The facial appearance of the 2 patients was very similar. However, the Japanese boy lacked craniosynostosis and microcephaly which were prominent findings in both the Newbury-Ecob baby and the South African boy.

There are sufficient phenotypic differences between both the subjects described by Newbury-Ecob et al. [1993] and Imaizumi and Kuroki [1991] to exclude these two syndromes from the diagnosis in our patient.

A search of the London Dysmorphology Database [Winter and Baraitser, 1992] documented a number of other syndromes with some overlap with that of our infant [Woon et al., 1980; Christian et al., 1971; Calabro et al., 1985; Pfeiffer et al., 1987]. However, the specific combination of anomalies present in this South African boy appears to be unique. Therefore we conclude that they represent a hitherto previously undelineated syndrome.

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